L1

L2

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(FILE 'HOME' ENTERED AT 13:32:46 ON 19 FEB 2004)

FILE 'DISSABS, 1MOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX, COMPUAB, CONF, CONFSCI, ELCOM, HEALSAFE, IMSDRUGCONF, LIFESCI, OCEAN, MEDICONF, PASCAL, PAPERCHEM2, POLLUAB, SOLIDSTATE, ADISCTI, ADISINSIGHT, ADISNEWS, ANABSTR, BIOBUSINESS, BIOCOMMERCE, ...' ENTERED AT 13:33:01 ON 19 FEB 2004

E JIAO JIN-AN?/AU
E NIEVES ESPERANZA?/AU
18 S E1 OR E2
E LUEPSCHEN LAWRENCE?/AU
108 S E1 OR E2 OR E9

E WONG HING?/AU

L3 2381 S ((TISSUE (A) FACTOR) OR TF) (A) (ANTI OR ANTIBOD?)
L4 92 S L3 (S) (H36 OR CH36 OR HFAT OR H36.D2.B7 OR HB-12255)

L5 84 DUP REM L4 (8 DUPLICATES REMOVED)

ANSWER 5 OF 84 IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 5 L5

10338222 IFIPAT; IFIUDB; IFICDB AN

ANTIBODIES FOR INHIBITING BLOOD COAGULATION AND TITLE:

METHODS OF USE THEREOF

Jiao; Jin-An, Fort Lauderdale, FL, US INVENTOR(S):

Luepschen; Lawrence, Miami, FL, US

Nieves; Esperanza Liliana, Plantation, FL, US

Wong; Hing C., Fort Lauderdale, FL, US

Sunol Molecular Corporation, Miami, FL, US

PATENT ASSIGNEE(S): EDWARDS & ANGELL, LLP, P.O. BOX 9169, BOSTON, MA,

02209, US

PK DATE NUMBER PATENT INFORMATION: US 2003082636 A1 20030501 APPLICATION INFORMATION: US 2002-293417 20021112

APPLN. NUMBER DATE
US 1997-814806 19970310 5986065
1999-293854 19990416 PENDING
20030501 GRANTED PATENT NO. DATE OR STATUS ------

CONTINUATION OF: CONTINUATION OF: FAMILY INFORMATION:

DOCUMENT TYPE: Utility

AGENT:

Patent Application - First Publication

CHEMICAL FILE SEGMENT:

APPLICATION

36 8 Figure(s). NUMBER OF CLAIMS:

DESCRIPTION OF FIGURES:

FIGS. 1A and 1B shows the nucleic acid (SEQ ID NOS: 1 and 3) and amino acid (SEQ ID NOS: 2 and 4) sequences of light chain and heavy chain variable regions H36.D2.B7 with hypervariable regions (CDRs or

Complementarity Determining Regions) underlined (single underline for nucleic acid sequences and double underline for amino acid sequences).

FIG. 2 shows association (Ka) and disassociation (Kd) constants of anti

-tissue factor antibodies as determined by ELISA

or BIACore analysis. FIG. 3 shows inhibition of TF:VIIa complex mediated FX activation by

pre-incubation with anti-tissue factor ***antibodies.***

FIG. 4 shows inhibition of TF/VIIa activity toward the FVIIaspecific substrate S-2288 by anti-tissue factor antibodies

FIG. 5 shows the capacity of the H36 antibody to increase prothrombin time (PT) in a TF-initiated coagulation assay.

FIGS. 6A and 6B graphically show the relationship between FXa formation and molar ratio of the H36.D2 antibody and rHTF. FIG. 6A: H36

.D2 was pre-incubated with the FT:VIIa complex prior to adding FX. FIG. 6B: ***H36.*** D2, TF:VIIa and FX were added simultaneously.

FIG. 7 shows inhibition of TF:VIIa activity by the H36.D2 antibody in a J-82 cell activation assay.

FIGS. 8A and 8B are representations of dot blots showing that the H36 .D2 antibody binds a conformational epitope on rhTF. Lane 1-native rHTF, Lane 2-native rhTF treated with 8M urea, Lane 3-native rHTF treated with 8M urea and 5 mM DTT. In FIG. 8A, the blot was exposed for approximately 40 seconds, whereas in FIG. 8B, the blot was exposed for 120 seconds.

The invention includes antibodies that provide superior anticoagulant activity by binding native human TF with high affinity and specificity. Antibodies of the invention can effectively inhibit blood coagulation in vivo. Antibodies of the invention can bind native human TF, either alone or present in a TF:VIIa complex, effectively preventing factor X binding to TF or that complex, and thereby reducing blood coagulation. Preferred antibodies of the invention specifically bind a conformational epitope predominant to native human TF, which epitope provides an unexpectedly strong antibody binding site.

L5 ANSWER 10 OF 84 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: DOCUMENT NUMBER:

2001:264665 BIOSIS PREV200100264665

TITLE:

Antibody-dependent cellular cytotoxicity and antibody

dependent cellular phygocytosis of breast cancer cells mediated by anti-tissue factor monoclonal antibodies.

AUTHOR(S):

Wen, Jinghai [Reprint author]; Jiao, Jin-An [Reprint author]; Zhu, Xiao-Yun [Reprint author]; Wong, Hing C.

[Reprint author]

CORPORATE SOURCE:

Sunol Molecular Corp., 2810 N Commerce Parkway, Miramar,

FL, 33025, USA

SOURCE:

FASEB Journal, (March 8, 2001) Vol. 15, No. 5, pp. A1198.

print.

Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001. Orlando, Florida, USA. March 31-April 04, 2001.

CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE:

Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE:

English

ENTRY DATE:

Entered STN: 30 May 2001

Last Updated on STN: 19 Feb 2002

Tissue factor (TF), an initiator of the extrinsic coagulation cascade, is AB expressed in a variety of tumor cells and plays an important role in tumor metastasis and progression. We have developed and produced an anti-human TF monoclonal antibody (H36), which has high affinity for human TF and potently inhibits TF function. A chimeric form (cH36) of H36 was constructed by fusing the Fc domain of the human IgG1 with the variable regions of the murine anti-TF antibody and expressed in a mammalian system with an aim to investigate the effects of these antibodies on human tumor growth in vitro and in vivo. Results have indicated that both H36 and cH36 are able to lyse TF positive breast cancer cells, such as MDA-MB-231, in antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phygocytosis (ADCP) assays. Animal studies also demonstrated that the H36 antibody is very effective against metastasis of human melanoma in nude mice. These data suggest that anti-TF antibody could be an effective anti-tumor agent in human immunotherapy.

ANSWER 8 OF 84 IFIPAT COPYRIGHT 2004 IFI on STN DUPLICATE 6 L_5

10224650 IFIPAT; IFIUDB; IFICDB AN

TITLE: ANTIBODIES FOR INHIBITING BLOOD COAGULATION AND

METHODS OF USE THEREOF

JIAO; JIN-AN, FORT LAUDERDALE, FL, US INVENTOR(S):

WONG; HING C., FORT LAUDERDALE, FL, US

PATENT ASSIGNEE(S): Unassigned

PATENT ASSIGNEE PROBABLE: Sunol Molecular Corp (Probable)

DIKE, BRONSTEIN, ROBERTS AND CUSHMAN, LLP EDWARDS AND AGENT:

ANGELL, LLP, 130 WATER STREET BOSTON, MA, 02109, US

PK DATE NUMBER PATENT INFORMATION: US 2002168357 A1 20021114 APPLICATION INFORMATION: US 1999-293854 19990416

> GRANTED PATENT NO. DATE OR STATUS APPLN. NUMBER

> > ----

US 1997-814806 19970310 5986065 CONTINUATION OF:

US 2002168357 FAMILY INFORMATION: 20021114

US 5986065

20030429 US 6555319

DOCUMENT TYPE: Utility

Patent Application - First Publication

FILE SEGMENT: CHEMICAL APPLICATION

36 8 Figure(s). NUMBER OF CLAIMS:

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or BIACore analysis.

FIG. 3 shows inhibition of TF:VIIa complex mediated FX activation by pre-incubation with anti-tissue factor ***antibodies.***

FIG. 4 shows inhibition of TF/VIIa activity toward the FVIIaspecific substrate S-2288 by anti-tissue factor antibodies

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The invention includes antibodies that provide superior anticoagulant activity by binding native human TF with high affinity and specificity. Antibodies of the invention can effectively inhibit blood coagulation in vivo. Antibodies of the invention can bind native human TF, either alone or present in a TF:VIIa complex, effectively preventing factor X binding to TF or that complex, and thereby reducing blood coagulation. Preferred antibodies of the invention specifically bind a conformational epitope

predominant to native human TF, which epitope provides an unexpectedly strong antibody binding site.